



**PATENT**  
**Attorney Docket No.: 18184-0002 CI1**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

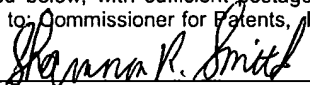
|                 |                                     |                    |
|-----------------|-------------------------------------|--------------------|
| In re:          | Patent application of               | :                  |
|                 | Robert F. Kucharik, <i>et al.</i>   | :                  |
|                 |                                     | :                  |
|                 |                                     | : Group Art Unit:  |
| Application No. | 10/727,940                          | : 1614             |
|                 |                                     | :                  |
| Filed:          | December 3, 2003                    | : Examiner:        |
|                 |                                     | : Not Yet Assigned |
|                 |                                     | :                  |
| For:            | TREATMENT OF INFLAMMATORY           | :                  |
|                 | DISORDERS WITH 2,3- BENZODIAZEPINES | :                  |
|                 |                                     | :                  |

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

**INFORMATION DISCLOSURE STATEMENT**

Sir:

Pursuant to 37 C.F.R. § 1.56 and in accordance with 37 C.F.R. §§ 1.97-1.98, the Applicants attach hereto a completed PTO Form-1449 (modified). This Information Disclosure Statement is being filed after three months following the filing date of this application but before the mailing date of the first Office Action on the merits. Therefore, no fee is believed to be due for this statement. However, authorization is provided to charge any fee deemed to be applicable to this filing to Deposit Account No. 50-0573.

|  |
|--|
| <b>CERTIFICATE OF MAILING</b><br><b>UNDER 37 C.F.R. 1.8(a)</b>   |
| I hereby certify that this paper, along with any paper referred to as being attached or enclosed, is being deposited with the United States Postal Service on the date indicated below, with sufficient postage, as first class mail, in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450. |
| BY: <br>SHANNON R. SMITH  |
| DATE: March 23, 2004   |

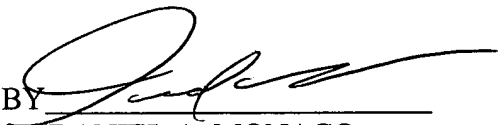
The Examiner is respectfully requested to review the items listed on the attached form and make them of record in the instant application as required by M.P.E.P. §609. It is requested that the Examiner initial the enclosed duplicate substitute PTO Form-1449, and return one copy to the undersigned.

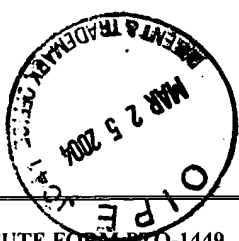
Pursuant to 37 CFR § 1.98(d), copies of the references listed in the Form PTO-1449 are not enclosed, since this patent application is a continuation-in-part of U.S. Application No. 10/309,573, filed December 3, 2002. Copies of the references are contained in the file of the earlier application. The Examiner should contact the undersigned if additional copies of any of the listed references are needed.

This Statement should not be construed as a representation that the cited references are material or that more relevant prior art does not exist.

Respectfully submitted,

ROBERT F. KUCHARIK, *et al.*

BY   
DANIEL A. MONACO  
Reg. No. 30,480  
DRINKER BIDDLE & REATH LLP  
One Logan Square  
18<sup>th</sup> and Cherry Streets  
Philadelphia, PA 19103-6996  
Tel.: (215) 988-3312  
Fax: 215) 988-2757  
*Attorney for the Applicants*



|   |  |                                 |                          |
|---|--|---------------------------------|--------------------------|
| SUBSTITUTE FORM PTO-1449<br><br><b>INFORMATION DISCLOSURE STATEMENT</b> | U.S. DEPARTMENT OF COMMERCE<br>PATENT AND TRADEMARK OFFICE | ATTY. DOCKET NO.<br>18184-2 C11 | SERIAL NO.<br>10/727,940 |
|   | APPLICANT:<br>Robert F. Kucharik, <i>et al.</i>            |                                 |                          |
|   | FILING DATE<br>December 3, 2003                            | GROUP<br>1614                   |                          |

**U.S. PATENT DOCUMENTS**

| EXAMINER<br>INITIAL |    | DOCUMENT<br>NUMBER | DATE     | NAME                  | CLASS | SUBCLASS | FILING DATE (IF<br>APPROPRIATE) |
|---------------------|----|--------------------|----------|-----------------------|-------|----------|---------------------------------|
|                     | AA | 3,736,315          | 5/29/83  | Jéno Kórosi et al.    | 540   | 567      |                                 |
|                     | AB | 4,322,346          | 3/30/82  | Jéno Kórosi et al.    | 540   | 567      |                                 |
|                     | AC | 4,423,044          | 12/27/83 | Jéno Kórosi et al.    | 514   | 221      |                                 |
|                     | AD | 4,614,740          | 9/30/86  | Tibor Láng et al.     | 514   | 221      |                                 |
|                     | AE | 4,835,152          | 5/30/89  | Jéno Kórosi et al.    | 514   | 220      |                                 |
|                     | AF | 4,840,948          | 6/20/89  | Tibor Láng et al.     | 514   | 221      |                                 |
|                     | AG | 5,204,343          | 4/20/93  | Ferenc András et al.  | 514   | 221      |                                 |
|                     | AH | 5,288,863          | 2/22/94  | György Somogyi et al. | 540   | 567      |                                 |
|                     | AI | 5,459,137          | 10/17/95 | Ferenc András et al.  | 514   | 220      |                                 |
|                     | AJ | 5,519,019          | 5/21/96  | Ferenc András et al.  | 514   | 220      |                                 |
|                     | AK | 5,521,174          | 5/28/96  | Ferenc András et al.  | 514   | 220      |                                 |
|                     | AL | 5,639,751          | 6/17/97  | Ferenc András et al.  | 514   | 220      |                                 |
|                     | AM | 5,891,871          | 4/6/99   | Haiji Xia et al.      | 514   | 219      |                                 |
|                     | AN | 6,075,018          | 6/13/00  | Pál Vágó et al.       | 514   | 221      |                                 |
|                     | AO | 6,080,736          | 6/27/00  | Donald W. Landry      | 514   | 221      |                                 |

**FOREIGN PATENT DOCUMENTS**

|  |    | DOCUMENT<br>NO. | DATE    | COUNTRY | CLASS | SUBCLASS | TRANSLATION |    |
|--|----|-----------------|---------|---------|-------|----------|-------------|----|
|  |    |                 |         |         |       |          | YES         | NO |
|  | AP | 0 492 485 A1    | 7/1/92  | Europe  |       |          |             |    |
|  | AQ | 178516          | 3/31/83 | Hungary |       |          | X           |    |
|  | AR | WO 92/11262     | 7/9/92  | PCT     |       |          |             |    |
|  | AS | WO 00/24400     | 5/4/00  | PCT     |       |          |             |    |

**EXAMINER****DATE CONSIDERED**

**EXAMINER:** Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

|   |  |                                 |
|---|--|---------------------------------|
| SUBSTITUTE FORM PTO-1449<br>U.S. DEPARTMENT OF COMMERCE<br>PATENT AND TRADEMARK OFFICE<br><br><b>INFORMATION DISCLOSURE STATEMENT</b> | <b>ATTY. DOCKET NO.</b><br>18184-2 C11                 | <b>SERIAL NO.</b><br>10/727,940 |
|   | <b>APPLICANT:</b><br>Robert F. Kucharik, <i>et al.</i> |                                 |
|   | <b>FILING DATE</b><br>December 3, 2003                 | <b>GROUP</b><br>1614            |

**OTHER DOCUMENTS** (Including Author, Title, Date, Pertinent Pages, Etc.)

|    |  |
|----|--|
| AT | Don E. Griswold et al., "Technique for Quantification of LTB <sub>4</sub> -Induced Changes in Peripheral Granulocyte Counts In Vivo in the Rabbit", Journal of Pharmacological Methods 25, 319-328 (1991).   |
| AU | F. Gatta et al., "Derivatives of 2,3-Benzodiazepine (*)", Il Farmaco - Ed. Sc. - vol. 40 - fasc. 12, pages 942-955.  |
| AV | R. Sladká et al., "A Placebo-controlled Clinical Trial with Tofizopam * in the Treatment of Anxiety Neurosis" Divisions of Psychiatry, District Institutes of National Health, Prague, 2 and 4; Psychiatric Department and Psychiatric Research Unity, Medical Scholl of Charles University, Prague, Czechoslovakia, pages 176-180 |
| AW | Edit J. Horváth et al., "Anxiolytic 2,3-benzodiazepines, their Specific Binding to the Basal Ganglia", Progress in Neurobiology Vol. 60 (2000), pages 309-342.   |
| AX | E. Tomori et al., "Investigation of the Metabolites of Tofizopam in Man and Animals by Gas-Liquid Chromatography-Mass Spectrometry", Journal of Chromatography, 241 (1982), pages 89-99.   |
| AY | Eva Tomori et al., "Investigation of Metabolites of Tofizopam in Man and Animals", Polish Journal of Pharmacology and Pharmacy, 1984, 36, pages 423-430., PL ISSN 0301-0214.   |
| AZ | Sharon Pellow et al., "The Effects of Tofisopam, a 3,4-Benzodiazepine, in Animal Models of Anxiety, Sedation, and Convulsions", Drug Development Research 7, pages 61-73 (1986).   |
| BA | A. Bond et al., "A Comparison of the Psychotropic Profiles of Tofisopam and Diazepam", Eur J Clin Pharmacol (1982) 22, pages 137-142.  |
| BB | B.S. Tsai et al., "The Leukotriene B <sub>4</sub> Receptor Agonist/Antagonist Activities of SC-45694 in Human Neutrophils", The Journal of Pharmacology and Experimental Therapeutics, Vol. 268, No. 3, 1994, pages 1493-1498.   |
| BC | Olu Oyesanmi, M.D. et al., "Hematologic Side Effects of Psychotropics", Psychosomatics 1999 40, pages 414-421.   |
| BD | J. Kanto et al., "Tofizopam: A Benzodiazepine Derivative Without Sedative Effect", International Journal of Clinical Pharmacology, Therapy and Toxicology, Vol. 20 No. 7 - 1982, pages 309-312.  |
| BE | T. Mennini et al., "Brain Levels of Tofizopam in the Rat and Relationship with Benzodiazepine Receptors", Naunyn-Schmiedeberg's Arch Pharmacol (1982) 321, pages 112-115.  |
| BF | K. Maier et al., "The Effect of Tofisopam on Psychic Performance in Persons with More than Average Anxiety: A Controlled Experimental Trial", Current Therapeutic Research, Vol. 35, No. 4, April 1984, pages 541-548.   |
| BG | Chihiro ITO, "Behavioral Pharmacological Study of the Structure-Activity Relationship of Benzodiazepine Derivatives - with Particular Reference to the Activity of 2,3-Benzodiazepine-, (1981) 39(3), pages 369-384 (Japanese), pages 1-30 (English Translation).  |

**EXAMINER****DATE CONSIDERED**

**EXAMINER:** Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

|                                  |  |   |                          |
|----------------------------------|--|---|--------------------------|
| SUBSTITUTE FORM PTO-1449         | U.S. DEPARTMENT OF COMMERCE<br>PATENT AND TRADEMARK OFFICE | ATTY. DOCKET NO.<br>18184-2 C11                 | SERIAL NO.<br>10/727,940 |
| INFORMATION DISCLOSURE STATEMENT |  | APPLICANT:<br>Robert F. Kucharik, <i>et al.</i> |                          |
|                                  |  | FILING DATE<br>December 3, 2003                 | GROUP<br>1614            |

## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

|    |  |
|----|--|
| BH | Milena Rizzo, "Chromatographic Separation of 2, 3-Benzodiazepines", Journal of Chromatography B, 747 (2000), pages 203-216.  |
| BI | Miklos Simonyi et al., "Stereoselective Binding of a 2,3-Benzodiazepine to Human Serum Albumin", Biochemical Pharmacology, Vol. 32, No. 12, (1983), pages 1917-1920.   |
| BJ | Giovambattista De Sarro et al., "GYKI 52466 and Related 2,3-Benzodiazepines as Anticonvulsant Agents in DBA/2 Mice", European Journal of Pharmacology 294 (1995), pages 411-422.   |
| BK | T. Seppälä, "Tofisopam, A Novel 3,4-Benzodiazepine: Multiple-Dose Effects on Psychomotor Skills and Memory. Comparison with Diazepam and Interactions with Ethanol", Psychopharmacology 69, (1980), pages 209-218.                       |
| BL | Veijo Saano et al., "Tofizopam Modulates the Affinity of Benzodiazepine Receptors in the Rat Brain", Pharmacology Biochemistry & Behavior, Vol. 17, (1982), pages 367-369.   |
| BM | Sharon Pellow et al., "The Effects of Tofisopam, a 3,4-Benzodiazepine, in Animal Models of Anxiety, Sedation, and Convulsions", Drug Development Research 7 (1986), pages 61-73.   |
| BN | A. Pakkanen et al., "Comparative Study of the Clinical Effects of Tofizopam, Nitrazepam and Placebo as Oral Premedication", British Journal of Anaesthetics, pages 1009-1012.  |
| BO | V. Saano et al., "Tofizopam Enhances the Action of Diazepam Against Tremor and Convulsions", Medical Biology 61: (1983), pages 49-53.  |
| BP | V. Saano et al., "Tofizopam Selectively Increases the Action of Anticonvulsants", Medical Biology, 64 (1986), pages 201-206.   |
| BQ | E.-E. Claesson, "Stimulation of Human Myelopoiesis by Leurotriene 8", Biochemical and Biophysical Research Communications, Vol. 131, No. 2 (1985), pages 579-585.  |
| BR | Julia Visy et al., "The Role of Configuration and Conformation in the Binding of 2,3-Benzodiazepines to Human Serum Albumin", CHIRALITY 1 (1989), pages 271-275.   |
| BS | István Tarnawa et al., "Structure-Activity Relationships of 2,3-Benzodiazepine Compounds with Glutamate Antagonistic Action", Bioorganic & Medical Chemistry Letters, Vol. 3, No. 1, (1993), pages 99-104.                               |
| BT | Sergey V. Kalashnikov et al., "Immunomodulating Effects of Tofizopam (Grandaxin®) and Diazepam in Vitro", Mediators of Inflammation, Vol. 11, (2002), pages 53-59.   |
| BU | Fogassy E. et al., "Studies on the Properties and Structure of Optically Active 1-(3,4-Dimethoxyphenyl)-4-Methyl-5-Ethyl-7,8-Dimethoxy-5H-2,3-Benzodiazepine (Tofizopam)", Studies in Organic Chemistry, Vol. 18, (1984), pages 229-233. |

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

|                                  |  |   |                          |
|----------------------------------|--|---|--------------------------|
| SUBSTITUTE FORM PTO-1449         | U.S. DEPARTMENT OF COMMERCE<br>PATENT AND TRADEMARK OFFICE | ATTY. DOCKET NO.<br>18184-2 C11                 | SERIAL NO.<br>10/727,940 |
| INFORMATION DISCLOSURE STATEMENT |  | APPLICANT:<br>Robert F. Kucharik, <i>et al.</i> |                          |
|                                  |  | FILING DATE<br>December 3, 2003                 | GROUP<br>1614            |

## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

|    |   |
|----|---|
| BV | Mark A. Jagels et al., "Neutrophil Chemotactic Factors Promote Leukocytosis", The Journal of Immunology, Vol. 148, No. 4, February 1992, pages 1119-1128.   |
| BW | K. Yamaguchi et al., "Tofisopam, A New 2,3-Benzodiazepine. Inhibition of Changes Induced by Stress Loading and Hypothalamic Stimulation", Can. J. Physiol Pharmacol, Vol. 61, (1983), pages 619-625.                  |
| BX | Szegő Judit et al., "Selected Passages From the Clinical-Pharmacological and Clinical Trials of Grandaxin®, "Acta Pharmaceutica Hungarica Vol. 63, (1993), pages 91-98 (Hungarian). Pages 1-10 (English Translation). |
| BY | L. Petőcz et al., "The Main Pharmacological Characteristics of Grandaxin (Tofizopam, Egyt-341), Hungarian Medical Journal, Vol. 23, No. 4, (1975), pages 134-138.   |
| BZ | Petőcz Lujza, "The Pharmacological Effects of Tofizopam (Grandaxin)®", Acta Pharmaceutica Hungarica, Vol. 63, (1993), pages 79-82 (Hungarian. Pages 1-4 (English Translation)..                                       |

|   |                 |
|---|-----------------|
| EXAMINER  | DATE CONSIDERED |
| EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. |                 |